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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/693,722

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Jerome B. Zeldis

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JONES DAY  
222 EAST 41ST ST  
NEW YORK, NY 10017

EXAMINER

OLSON, ERIC

ART UNIT

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/693,722	<b>Applicant(s)</b> ZELDIS ET AL.	
	<b>Examiner</b> ERIC S. OLSON	<b>Art Unit</b> 1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 12 December 2007.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-5, 9, 23, and 27-34 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-5, 9, 23 and 27-34 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

### **Detailed Action**

This office action is a response to applicant's communication submitted December 12, 2007 wherein the rejections of record in the previous office action are traversed. This application claims benefit of provisional application 60/421004, filed October 24, 2002.

Claims 1-5, 9, 23, and 27-34 are pending in this application.

Claims 1-5, 9, 23, and 27-34 as amended are examined on the merits herein.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on December 12, 2007 has been entered.

The following rejections of record in the previous office action are maintained:

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 9, and 27-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Omoigui (US patent publication 20040038874, of record in previous action) in view of Muller et al. (US patent 6020358, of record in previous action)

Omoigui discloses a method for the treatment of persistent pain by administering a drug that antagonizes one or more mediators of inflammation. (p. 1, paragraph 0004) Drugs useful in this manner include TNF- $\alpha$  blockers (p. 2, paragraphs 0007 and 0011) including thalidomide and thalidomide analogs. (p. 3, paragraph 0023) Reflex Sympathetic Dystrophy, otherwise known as chronic regional pain syndrome, is listed as a disease treatable by this method. (pp. 9-10, paragraphs 0078-0082)

Omoigui does not disclose a therapeutic method comprising administering the specific TNF- $\alpha$  inhibitor (+)-2-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonyl-ethyl]-4-acetylaminoisoindolone-1,3-dione, or one involving a pharmaceutical dosage form having the specific limitations of instant claims 28-34.

Muller et al. discloses that compounds of a general formula including that of the claimed compound (column 5, line 1) are capable of decreasing the levels of TNF- $\alpha$  in a patient, (column 4, lines 55-67) thus qualifying as a TNF- $\alpha$  blocker. Example 12 (column 14, lines 35-55) is the exact same compound (+)-2-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonyl-ethyl]-4-acetylaminoisoindolone-1,3-dione disclosed in the instant claims. Muller et al. also discloses oral dosage forms of this compound as tablets or capsules, having a unit dosage of 1-100 mg, along with another dosage form in isotonic saline, a pharmaceutically acceptable solvate. (column 9, lines 22-52) Muller et al. also discloses that this chiral compound can be isolated as individual isomers and

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used in the disclosed invention, and additionally suggests methods for isolating the isomers. (column 8 line 63 - column 9 line 12)

It would have been obvious to one of ordinary skill in the art at the time of the invention to use the compound of example 12 of Muller et al. in the method of Omoigui, in an appropriate dosage form as disclosed by Muller et al. One of ordinary skill in the art would have been motivated to use this compound and dosage form because it is disclosed by Muller et al. to be useful for lowering TNF- $\alpha$  levels in a subject. One of ordinary skill in the art would reasonably have expected success because the scope of Omoigui includes all compounds capable of inhibiting or otherwise blocking the activity of TNF- $\alpha$ .

Thus the invention taken as a whole is *prima facie* obvious.

Response to Argument: Applicant's arguments, submitted December 12, 2007, have been fully considered as regards the above grounds of rejection and not found to be persuasive to remove the rejection. Applicant argues that there is not significant structural similarity between the compounds of Muller et al. and Omoigui et al. to support using the compounds of Muller et al. in the method of Omoigui et al. However, the combination is primarily based upon a shared biological function (as TNF-alpha blockers) rather than on a structural similarity. Structural similarity is invoked only to demonstrate that one of ordinary skill in the art would have considered these compounds to be thalidomide analogs according to Omoigui et al.

Applicant further argues that the compound described by Muller et al. is described as a racemate, and that isolating and using the individual enantiomers is not

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obvious in view of the racemate. However, as discussed above, Muller et al. specifically suggests isolating the enantiomers and using them as therapeutic agents, and furthermore suggests using chiral chromatography or chiral salt formation to do so. Therefore Muller et al. already discloses the individual enantiomers.

Applicant also argues that there is no motivation to pick the specific combination of one compound and one disease recited in the instant claims from the long list of diseases and compounds recited in the prior art. However, according to MPEP 2145, “the prior art’s mere disclosure of more than one alternative does not constitute a teaching away from any of these alternatives because such disclosure does not criticize, discredit, or otherwise discourage the solution claimed...” In re Fulton, 391 F.3d 1195, 1201, 73 USPQ2d 1141, 1146 (Fed. Cir. 2004). Therefore each and every disease species of Omoigui et al. and each and every compound of Muller et al. is considered to be disclosed by the prior art, and using any of the known TNF-alpha blockers of Muller et al. to treat any of the diseases revealed by Omoigui et al. to be treatable by blocking TNF-alpha is merely an obvious variation of the prior art.

Finally, Applicant argues that the prior art discloses a selection of numerous compounds, and that one of ordinary skill in the art would not expect that the selection of a single compound from a large number disclosed by Muller et al. would be suitable for a method of treating complex regional pain syndrome. According to *KSR v. Teleflex INC*, “When there is a design need or marked pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill in the art has good reason to pursue the known options within his or her technical grasp. If this

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leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under §103.” (p. 15, second paragraph) See *KSR Intl Co v. Teleflex INC*, 82 USPQ2d 1385, 1396 (US 2007). In other words, one of ordinary skill in the art would have been able to, with only routine experimentation, test the various compounds of Muller et al. to determine which were suitable for use in a therapeutic method according to Omoigui et al.

For these reasons the rejection is deemed proper and maintained.

Claims 2-5 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Omoigui (US patent publication 20040038874, of record in previous action) in view of Muller et al. (US patent 6020358, of record in previous action) as applied to claims 1, 9, and 27-34 above, and further in view of Merck. (Reference of record in previous office action)

The disclosure of Omoigui in view of Muller et al. is discussed above. Omoigui in view of Muller et al. does not disclose a method further comprising administering the additional therapeutic agents of instant claims 2-5 or the therapies of instant claim 23.

Merck discloses that complex regional pain syndrome may be treated with several drugs including nifedipine, prednisone, opioid analgesics, tricyclic antidepressants, and anticonvulsants. (p. 1373, left column, second paragraph) It should be noted that it is well known in the art that opioid analgesics include oxycodone, tricyclic antidepressants include amitriptyline, imipramine, and doxepin, and

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anticonvulsants include gabapentin. Merck also discloses that physical therapy is essential throughout therapy for complex regional pain syndrome (p. 1373, left column, last paragraph) and that pain relief that outlasts the administration of a sympathetic block but is still transitory suggests the need for surgery. (p. 1373, left column, second paragraph)

It would have been obvious to one of ordinary skill in the art at the time of the invention to practice the method of Omoigui et al. for the treatment of complex regional pain syndrome further comprising administering one or more of the pharmaceutical active agents described by Merck and still further administering physical therapy and/or surgery. One of ordinary skill in the art would have been motivated to combine these teachings because Omoigui et al. and Merck both disclose their respective teaching as being useful for treating the same condition, namely complex regional pain syndrome. One of ordinary skill in the art would reasonably have expected success because combining two treatments known in the prior art to be effective for treating the same disorder by different methods is reasonably expected to produce at least additive effects.

Thus the invention taken as a whole is *prima facie* obvious.

Response to Argument: Applicant's arguments, submitted December 12, 2007, have been fully considered as regards the above grounds of rejection and not found to be persuasive to remove the rejection. Applicant's arguments with respect to this rejection are the same as those made with respect to the rejection over Omoigui et al. in



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view of Muller et al., and are not found to be persuasive for the same reasons.

Therefore the rejection is deemed proper and maintained.

### ***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 9, and 27 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over either claims 1, 6, 12, and 17 of U.S. Patent No. 6020358 (Reference of record in previous action, herein referred to as ‘358) or alternately claims 1, 4, 10, and 15 of U.S. Patent No. 6011050 (Reference cited in PTO-1449 July 26, 2004, herein referred to as ‘050) in view of Omoigui. (US patent publication 20040038874, Reference of record in previous action) Claim 17 of ‘358 and claim 15 of ‘050 are both drawn to methods of reducing undesirable levels of TNF- $\alpha$  in a

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mammal by administering a compound having a generic structure which includes within its breadth the species recited in instant claim 27. Claims 6 and 12 of '358 and 4 and 10 of '050 further suggest the claimed structure by defining R4, R5, and R6. Said claims do not disclose a method of treating neuropathic pain in this manner.

Omoigui discloses a method for the treatment of persistent pain by administering a drug that antagonizes one or more mediators of inflammation. (p. 1, paragraph 0004) Drugs useful in this manner include TNF- $\alpha$  blockers. (p. 2, paragraphs 0007 and 0011) Reflex Sympathetic Dystrophy, otherwise known as chronic regional pain syndrome, is listed as a disease treatable by this method. (pp. 9-10, paragraphs 0078-0082)

It would have been obvious to one of ordinary skill in the art at the time of the invention to practice the methods of Claim 17 of '358 and claim 15 of '050 on a mammal suffering from neuropathic pain caused by a herniated disk. One of ordinary skill in the art would have been motivated to practice the invention in this manner because claims 1, 21, and 27 of '250 disclose that blocking the action of TNF- $\alpha$  is an effective strategy for treating neuropathic pain in a herniated disk. One of ordinary skill in the art would have reasonably expected success because claims 1, 21, and 27 of '050 already demonstrate the utility of this method.

Response to Argument: Applicant's arguments, submitted December 12, 2007, have been fully considered as regards the above grounds of rejection and not found to be persuasive to remove the rejection. Applicant argues that the claims of '358 and '050 do not disclose the specific compound, having a specific combination of substituents, that is claimed in the claimed invention. However, as the claimed structure

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in '358 and '050 is a closed set with specific, well-defined substituents selected from a finite, limited list, one of ordinary skill in the art would have recognized it as reciting a finite list of definite compounds, just like a Markush group having a large but definite number of members. As discussed above, according to MPEP 2145, “the prior art’s mere disclosure of more than one alternative does not constitute a teaching away from any of these alternatives because such disclosure does not criticize, discredit, or otherwise discourage the solution claimed....” *In re Fulton*, 391 F.3d 1195, 1201, 73 USPQ2d 1141, 1146 (Fed. Cir. 2004).

Applicant further argues that one of ordinary skill in the art would not have been motivated to select the particular disease species of complex regional pain syndrome from the list of diseases recited by Omoigui et al. Again, the number of different species recited by a reference does not render any individual species unavailable to one of ordinary skill in the art. One of ordinary skill in the art would have seen the Omoigui reference as teaching that a method of reducing TNF-alpha levels, such as that claimed in '358 and '050, is therefore useful for treating any of the diseases discussed by Omoigui.

For these reasons the rejection is deemed proper and maintained.

### ***Conclusion***

No claims are allowed in this application.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eric S. Olson whose telephone number is 571-272-9051. The examiner can normally be reached on Monday-Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on (571)272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Eric S Olson/  
Examiner, Art Unit 1623  
2/19/2008

/Shaojia Anna Jiang/  
Supervisory Patent Examiner, Art Unit 1623